FORM PTO-1390 (REV 11-98) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER	
17224(AP)	
U.S. APPLICATION NO. (If known, see 37 CFR 1.5)	
09/367712	
INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE
PCT/US98/03355	20 February 1998
PRIORITY DATE CLAIMED	
20 February 1997	

TITLE OF INVENTION
TAZAROTENE AND CORTICOSTEROID TREATMENT FOR PSORIASIS

APPLICANT(S) FOR DO/EO/US
Allergan Sales, Inc.

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [ ] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. [X] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [ ] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] has been transmitted by the International Bureau.
   c. [X] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [ ] A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. [X] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [X] have not been made and will not be made.
8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. [ ] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. [ ] An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [ ] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.
16. [X] Other items or information:

Copy of Assignment of Assignor's Interest recorded September 3, 1998 on Reel 9429, Frame 0205 consisting of four pages.

X Copy of PCT General Power of Attorney
X FORMAL DRAWINGS (2 Sheets) (2 sets)

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO	ATTORNEY'S DOCKET NUMBER
09/367712	PCT/US98/03355	17224 (AP)

	CALCULATIONS PTO USE ONLY	
17. ☒ The following fees are submitted:		
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$970.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$840.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$760.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$670.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) **$96.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 840.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	11 - 20 =		X $18.00	$	
Independent claims	2 - 3 =		X $78.00	$	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $260.00	$	
TOTAL OF ABOVE CALCULATIONS =				$	
Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement must also by filed (Note 37 CFR 1.9, 1.27, 1.28).				$	
SUBTOTAL =				$ 840.00	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +				$	
TOTAL NATIONAL FEE =				$ 840.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +				$	
TOTAL FEES ENCLOSED =				$ 840.00	
				Amount to be: refunded	$
				charged	$

a. ☐ A check in the amount of $_____ to cover the above fees is enclosed.

b. ☒ Please charge my Deposit Account No. 01-0885 in the amount of $ 840.00 to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 01-0885. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

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REGISTRATION NUMBER

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17224(AP)PCT

TAZAROTENE AND CORTICOSTEROID TREATMENT FOR PSORIASIS

CROSS REFERENCE TO RELATED APPLICATIONS

This patent application claims priority from Provisional Patent Application 60/03915 filed on February 20, 1997.

BACKGROUND OF THE INVENTION

1. FIELD OF THE INVENTION

This invention relates to pharmaceutical compositions for application to the skin and to a method for the treatment of proliferating skin diseases. The composition may be applied topically. The treatment can be either therapeutic or prophylactic.

2. DESCRIPTION OF RELATED ART

Proliferative skin diseases are widespread throughout the world and afflict millions of humans and their domesticated animals. This invention provides a method for treatment of such diseases. As used hereinafter in this specification and in the claims, the expression "proliferative skin diseases" means benign and malignant proliferative skin diseases which are characterized by accelerated cell division in the epidermis, dermis or appendages thereto, associated with incomplete tissue differentiation. Such diseases include: psoriasis, atopic dermatitis, non-specific dermatitis, primary irritant contact dermatitis, allergic contact dermatitis, basal and squamous cell carcinomas of the skin, lamellar ichthyosis, epidermolytic hyperkeratosis, premalignant sun-induced keratosis, non-malignant

keratosis, acne, and seborrhic dermatitis in humans and atopic dermatitis in domesticated animals.

Heretofore, proliferative skin diseases have been generally accepted by mankind as an ongoing evil having degrees of severity variable with inherited skin traits and external factors but always have been recognized as unsightly, painful, morbid diseases. Over the history of mankind innumerable medicines and treatments have been proposed, tried and used with varying degrees of success.

Treatments which are prescribed and used for the treatment of proliferative skin diseases include the following:

(1) topical applications, e.g. coal tar derivatives, 5-fluorouracil, vitamin A acid, glucocorticoids in high dosage, bath oils and non-specific emollient creams and ointments;

(2) systemic administration, e.g. glucocorticoids and classic anti-cancer agents, for example, methothrexate, hydroxyurea, azaribine, cyclophosphamide; and

(3) physical modalities, e.g. ultra violet light, x-radiation, and, in severe cases, surgery.

While these treatments provide, in certain cases some remission of the original symptoms, each treatment suffers some defect, for example, temporary and incomplete mitigation of symptoms, rapid re-occurrence of the disease when mitigation is terminated, serious and sometimes irreversible damage (atrophy) resulting from the topical application for extended times of glucocorticoids, acute bone marrow suppression, cirrhosis of the liver resulting from the protracted use of methothrexate which may lead to death of the patient, and the causation of cancer by the application of anti-cancer drugs, x-radiation, or ultra violet rays.

Recently, a new compound has been approved by the Food and Drug Administration for the treatment of psoriasis and acne. Tazarotene. Tazarotene is available as Tazorac® 0.1% and Tazorac® 0.05% topical gel from Allergan, Inc. of Irvine, California.

BRIEF SUMMARY OF THE INVENTION

The present invention relates to a method of treating psoriasis in humans with tazarotene, preferably a gel comprising 0.1%, tazarotene by weight, and a corticosteroid, preferably a cream. The tazarotene gel may be administered once daily in the evening and the corticosteroid cream may be administered to the subject once daily in the morning, or the gel and cream may be administered on alternate days. The tazarotene gel is disclosed in U.S. patent Application Serial no. 623,184, which is entitled "Stable Gel Formulation for Topical Treatment of Skin Conditions", which was filed on March 28, 1996, in the name of Prakash Charu and is hereby incorporated by reference in its entirety.

In one aspect of the invention, the corticosteroid may be Synalar® cream (0.01% fluocinolone acetonide), Elocon® cream (0.1% mometasone furoate) or Lidex® cream (0.05% fluocinonide), i.e. a low-potency, mid-potency and high-potency corticosteroid, respectively.

In another aspect of the invention, the corticosteroid may be fluocinonide 0.05% ointment, Lidex®, a high potency steroid, mometasone fuoate 0.1% ointment, Elocon®, a high potency steroid, diflorasone diacetate 0.05% ointment, Maxiflor®, a high potency steroid, fluticasone propionate 0.005% ointment, Cultivate®, a mid-potency steroid, betamethasone dipropionate 0.05% cream, Diprosone®, a mid-potency steroid, diflorasone diacetate 0.05% cream, Maxiflor®, a mid-

potency steroid, clobetasol propionate 0.05% ointment, Temovate®, a super-potency steroid, betamethasone valerate 0.1% lotion, Valisone®, a mid-potency steroid.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a graph comparing the reduction in plaque elevation over a 12 week treatment period with tazarotene in combination with placebo, high-potency corticosteroid, mid-potency corticosteroid and low-potency corticosteroid.

Figure 2 shows the treatment success with the combination therapies of Figure 1.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with this invention it has been found that proliferative skin diseases are alleviated, that is, the symptoms of the disease are noticeably improved or become undetectable, by the treatment of the afflicted patient, or animal, with the pharmaceutical compounds described in detail, hereinbelow.

For the purposes of this specification and the claims, a proliferative skin disease is alleviated when there is a noticeable decrease in the thickness of a lesion to palpation, with or without residual redness, or residual slightly dilated blood vessels or residual hyper- or hypo-pigmentation. For purposes of this invention and the claims hereof, psoriasis is alleviated when a scale-free psoriasis lesion is noticeably decreased in thickness, or noticeably but incompletely cleared or completely cleared.

The compositions utilized in the method of this invention may be applied topically.

The term "topical" as employed herein relates to the use of the active ingredient incorporated in a suitable pharmaceutical carrier, and applied at the site of the disease for exertion of local action. Accordingly, such topical compositions include those pharmaceutical forms in which the compound is applied externally by direct contact with the skin surface to be treated. Conventional pharmaceutical forms for this purpose include ointments, lotions, pastes, jellies, sprays, aerosols, bath oils and the like. The term "ointment" embraces formulations (including creams) having oleaginous, absorption, water-soluble and emulsion-type bases, e.g., petroleum, lanolin, polyethylene glycols, as well as mixtures thereof. Topical application with occlusion of an area larger than the medicated area may produce improved results relative to non-occluded topical applications.

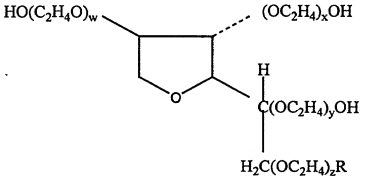
The percentage by w/w of the active ingredient, i.e. the corticosteroid herein utilized ranges from about 0.001% to about 1% of the pharmaceutical preparation, preferably from about 0.005% to about 0.1%, by weight.

The percentage by w/w of the active ingredient, i.e. tazarotene herein utilized ranges from about 0.01% to about 15% of the pharmaceutical preparation, preferably from about 0.1% to about 2% and in these preparations the aforesaid pharmaceutical carrier for topical application constitutes a major amount of the said preparation.

Preferably tazarotene is utilized as a stable gel formulation for topical treatment of skin conditions in humans, said stable gel formulation comprising: Ethyl-6-[2-(4,4-dimethylthiochroman-6-yl)ethynyl]nicotinate in a plurality of nonaqueous vehicles for both solubilizing tazarotene and forming a gel therewith, said nonaqueous vehicles enabling topical application of the gel to a skin condition, said plurality of vehicles each

being present in amounts, and in combination, to control release of tazarotene from the gel to the skin conditions. In the tazarotene formulation the vehicles are present in amounts selected to produce maximum release of the active agent, i.e. tazarotene, from the gel when all the vehicles are present therein. Preferably the formulation comprises three vehicles and more preferably the formulation comprises three vehicles which are used to both solubilize the active agent and form a gel.

The formulation preferably comprises the three vehicles, e.g. Polysorbate 40, Poloxamer 407 and Hexylene glycol. Polysorbate 40 is



wherein the Sum of w, x, y, and z is 20 and R is $(C_{15}H_{31})COO$ and Poloxamer 407 is $HO(C_2H_4O)_a(C_3H_6O)_b(C_2H_4O)_aH$ having the following properties.

USAN for Poloxamers

Poloxamer	Physical Form	Average Molecular Weight	Average Values a	Average Values b	BASF Corp. Brand Name
					Pluronic
124	Liquid	2090 to 2360	12	20	L 44
188	Solid	7680 to 9510	80	27	F 68
237	Solid	6840 to 8830	64	37	F 87
338	Solid	12700 to 17400	141	44	F 108
407	Solid	9840 to 14600	101	56	F 127

More preferably, tazarotene is utilized as a stable gel formulation for topical treatment of psoriasis comprising an effective amount of Ethyl-6-[2-(4,4-dimethylthiochroman-6-yl)ethynyl]nicotinate in a pharmaceutical carrier comprising:

(a) water;
(b) edetate disodium;
(c) ascorbic acid;
(d) Carbomer 934P;
(e) Poloxamer 407;
(f) polyethylene glycol;
(g) Polysorbate 40;
(h) hexylene glycol;
(i) butylated hydroxytoluene;
(j) butylated hydroxyanisole;

(k) benzyl alcohol; and

(l) tromethamine.

The tazarotene formulation may comprise Polysorbate 40 in an amount up to about 0.4% by weight, Poloxamer 407 in an amount up to about 0.4% by weight, and hexylene glycol in an amount up to about 2% by weight or more preferably Polysorbate 40, in an amount of about 0.32% by weight, Poloxamer 407 in an amount of about 0.18% by weight, and hexylene glycol in an amount of about 2% by weight.

Most preferably, the tazarotene formulation comprises:

INGREDIENT	FUNCTION	CONCENTRATION %W/W
tazarotene	Drug	0.1
purified water	Excipient	49.25
Edetate Disodium	Stabilizer	0.05
Ascorbic acid	Stabilizer	0.05
Carbomer 934P[1]	Thickening agent	1.25
Poloxamer 407	Surfactant	0.2
PEG-400	Co-solvent	45.0
Polysorbate 40	Surfactant	0.2
Hexylene glycol	Co-solvent	2.0
Butylated hydroxytoluene	Stabilizer	0.05
Butylated hydroxyanisole	Stabilizer	0.05
Benzyl alcohol	Preservative	1.0
Triethanolamine/ Tromethamine	Neutralizer	0.8

[1]Carbomer 934P [1975]. NF. The viscosity of a neutralized 0.5 percent aqueous dispersion of Carbomer 934P is between 29,400 and 39,400 centiposes. (1) Polymer of 2-propenoic acid, cross-linked with allyl ethers of sucrose or pentaerythritol; (2) Polymer of acrylic acid, cross-linked with allyl ethers of sucrose or pentaerythritol. Molecular weight is approximately 3,000,000.

The tazarotene formulation and the corticosteroid formulation, each, will be applied, topically, in an amount to achieve the maximum effect on alleviating the proliferative skin disease symptoms without causing an adverse reaction. Selection of such an amount of either formulation is well within the skill of the art.

Preferably, the tazarotene formulation is utilized to provide from about 0.5 to about 5 mg of tazarotene per cm^2 of affected skin, more preferably from about 1 to about 3 mg/cm^2, e.g. 2 mg/cm^2.

The method of this invention also employs a corticosteroid. The expression "corticosteroid" refers to a naturally occurring product of the adrenal cortex, or a synthetic analog thereof possessing anti-inflammatory activity and minimal or no mineralocorticoid activity or sex steroid activity. The corticosteroids include glucocorticoids. Of the natural glucocorticoids, one may use for example, hydrocortisone or the synthetic glucocorticoids such as methyl prednisolone acetate (Prednisone) or triamcinolone for topical therapy. The corticosteroids are preferably employed in amounts of from 0.5 to 5 mg per cm^2 of affected skin, more preferably from about 1 to 3 mg/cm^2, e.g. 2 mg/cm^2.

The treatment period may be 12 weeks with a 4 week follow-up period. The subjects are evaluated for plaque elevation, scaling and erythema with a successful treatment defined as about 50% improvement or better. During the treatment period, tazarotene in combination with the mid- or high-potency corticosteroid produced significantly better results than treatment with tazarotene in combination with placebo in reducing plaque elevation, scaling, erythema and overall severity. During the 4 week post-treatment period, the results with tazarotene plus mid- or high-potency corticosteroid were equal to or better than tazarotene plus placebo or tazarotene plus low-potency corticosteroid.

The most common adverse events resulting from the treatment were burning, pruritus and erythema; however there was a lower incidence of such adverse events in patients treated with tazarotene plus the medium- or high-potency corticosteroid.

Thus, treating psoriasis in humans with a combination of tazarotene and a mid-potency or high-potency corticosteroid is more effective than a combination of tazarotene and low-potency or placebo and results in a lower incidence of adverse events such as burning pruritis and erythema.

The invention is further illustrated by the following examples which are illustrative of various aspects of the invention, and are not intended as limiting the scope of the invention as defined by the appended claims.

EXAMPLE 1

The study reported here utilizes a combination regimen that alternates between tazarotene 0.1% gel and a corticosteroid or placebo cream every evening. The aim of the study was to determine whether such alternating therapy may offer clinical benefits by maximizing the therapeutic benefits of both drugs, while also minimizing corticosteroid use and thus reducing the potential for adverse corticosteroid-induced effects.

This study was a multicenter, investigator-masked, parallel-group study, enrolling 398 patients with stable plaque psoriasis. Topical applications of tazarotene 0.1% gel, were administered every other evening, and one of the following creams administered on alternate evenings): placebo; low-potency corticosteroid (hydrocortisone acetate 1%); medium-potency corticosteroid (alclometasone dipropionate 0.05%); or high-potency corticosteroid (betamethasone valerate 0.1%).

The study required a 12-week treatment period plus a 4-week follow-up phase. The patient demographics included 388 patients (231 male and 157 female) with evaluable data, mean age of 46.7 years (range: 21-88 years) and a mean duration of psoriasis of 17.39 years.

All treatment groups achieved clinically significant reductions in plaque elevation at all treatment and post-treatment visits, with the tazarotene/high-potency combination taz/high group achieving consistently greater reductions than

the other treatments throughout the study. At week 4, these reductions were significantly greater than those in all the other treatment groups. The taz/high also achieved clinically significant reductions in plaque elevation more rapidly than the other treatments, i.e. in two weeks compared with four weeks in all the other groups. (See the results set forth in Figure 1.)

Treatment success was defined as a moderate, marked, almost clear or completely cleared response ($\geq$ 50% global clinical improvement). All tazarotene/corticosteroid treatment groups achieved treatment success rates of > 50% within 4 weeks. However, the taz/high combination achieved significantly greater treatment success rates than the tazarotene/placebo (taz/plac) and tazarotene/medium-potency corticosteroid (taz/med) combinations throughout the 12-week treatment period. Peak treatment success rates ranged from 56% (for patients treated with taz/plac at Week 8) to 77% (for taz/high at Week 8).

During the 4-week follow-up period, all groups retained $\geq$ 60% global clinical improvements in psoriasis, with treatment success rates ranging from 60% (for taz/med) to 75% (for taz/high) at study Week 16. These improvements were statistically and clinically significant compared with the pretreatment levels and there were no significant differences between the groups at the end of the follow-up period. (See Figure 2.)

Week 12, the probability of patients being considered a treatment success at any study visit was 77% in the taz/high group. In the other groups the treatment success was 56 to 61%.

The taz/high combination also achieved initial treatment success significantly faster than any of the other combinations. The median time to treatment success was 2 weeks in the taz/high group, compared with 4 weeks in each of the other groups.

All treatment groups achieved clinically significant reductions in scaling during the treatment period, and the taz/high combination was consistently the most efficacious treatment throughout the 12-week treatment period. The reductions in

scaling achieved in all groups by the end of the treatment period were generally maintained during the 4-week follow up period.

All treatment groups achieved statistically significant reductions in erythema during the treatment period and, once again, the taz/high combination was the most efficacious treatment. During the follow-up period, all groups retained significant reductions in erythema compared with baseline levels, and these reductions were clinically significant in the taz/high, taz/med, and taz/plac groups.

The overall incidence of adverse events that were possibly, probably or definitely treatment-related decreased with increased corticosteroid potency, falling from 42% in the taz/plac group, to 36%, 32% and 31% in the tazarotene/low-potency corticosteroid (taz/low), taz/med, and taz/high groups, respectively. (See Table II, below.)

Table II. Overall incidence of adverse events

	Patients (%)			
	Taz/plac	Taz/low	Taz/med	Taz/high
Pruritus	15	19	16	8
Erythema	12	7	6	6
Irritation	8	9	5	4
Burning	6	4	4	8

In view of the above Example, the following conclusions may be drawn. Alternate-day treatment with tazarotene 0.1% gel and the high potency corticosteroid cream was consistently more effective than the other three regimens in reducing plaque elevation, scaling and erythema. Patients in the tazarotene plus high-potency corticosteroid group also achieved significantly higher treatment

success rates (≥ 50% global clinical improvement, and achieved treatment success faster, than patients in the other groups. Treatment-related adverse events comprised mainly mild to moderate local irritation including pruritus, erythema and burning skin. The incidence of treatment-related adverse events decreased as the potency of the corticosteroid cream used increased.

EXAMPLE 2

The study of Example 1 is substantially repeated with fluocinolone acetonide 0.01% cream (low-potency), mometasone furoate 0.1% cream (mid-potency) and fluocinonide 0.05% cream (high-potency) used as the corticosteroids. In this study tazarotene 0.1% gel in combination with a mid-potency or high-potency corticosteroid, when compared with tazarotene plus placebo cream, was associated with significantly higher treatment success rates, significantly greater reductions in scaling, erythema, and overall lesional severity, with a decreased incidence of adverse events. The corticosteroids are Synalar® cream, Elocon® cream and Lidex® cream, respectively.

While particular embodiments of the invention have been described, it will be understood of course that the invention is not limited thereto since many obvious modifications can be made and it is intended to include within this invention any such modifications as will fall within the scope of the appended claims.

Having now described the invention, I claim.

1. A method for treating proliferative skin diseases comprising the administration of an effective amount of tazarotene and an effective amount of a corticosteroid.

2. The method of claim 1 wherein said corticosteroid is selected from the group consisting of fluocinolone acetonide, mometasone furoate, fluocinonide, diflorasone diacetate, fluticasone propionate, betamethasone dipropionate, clobetasol propionate, betamethasone valerate.

3. The method of claim 1 wherein tazarotene is applied as a 0.1% gel.

4. The method of claim 1 wherein said corticosteroid is a mid- or high-potency corticosteroid.

5. The method of claim 4 wherein said corticosteroid is selected from the group consisting of mometasone furoate and fluocinolone acetonide.

6. A method for treating psoriasis in a human subject by topically applying to the psoriatic skin of said subject an effective amount of tazarotene and an effective amount of a corticosteroid.

7. The method of claim 6 wherein tazarotene is applied as a 0.1% gel.

8. The method of claim 7 wherein said corticosteriod is a cream.

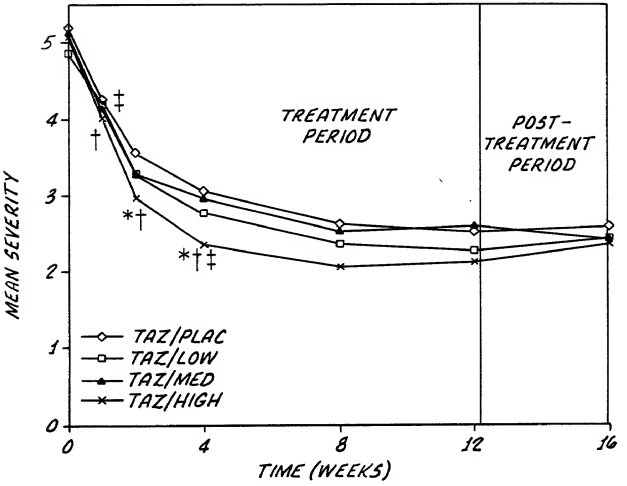
9. The method of claim 8 wherein said corticosteroid is a mid- or high-potency corticosteroid.

10. The method of claim 9 wherein said corticosteroid is selected from the group consisting of mometasone furoate and fluocinolone.

11. The method of claim 6 wherein tazarotene is administered once daily in the evening and the corticosteroid is administered once daily in the morning.

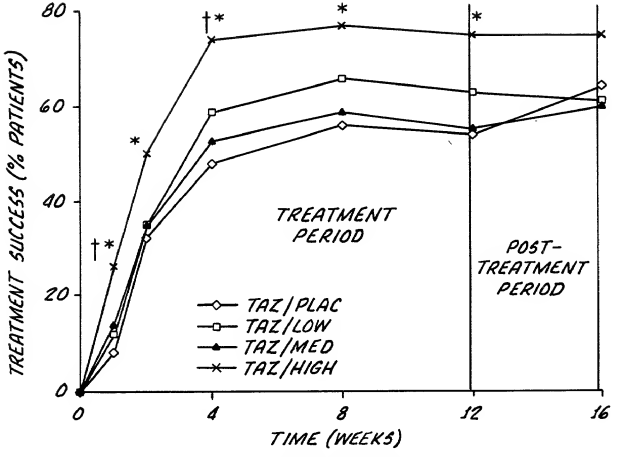
ABSTRACT

The present invention provides a method for treating proliferative skin diseases comprising the administration of an effective amount of tazarotene and an effective amount of a corticosteroid. This invention is especially useful for treating psoriasis.



*P < 0.05 VS TAZ/PLAC;
†P < 0.05 VS TAZ/LOW;
‡P < 0.05 VS TAZ/MED.

FIG. 1.



*P < 0.05 VS TAZ/PLAC AND TAZ/MED
†P < 0.05 VS TAZ/LOW

FIG. 2.

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PTO/SB/01 (12-97)
Approved for use through 9/30/00. OMB 0651-0032
Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63)

☒ Declaration Submitted with Initial Filing OR ☐ Declaration Submitted after Initial Filing (surcharge (37 CFR 1.16 (e)) required)

Attorney Docket Number	17224 (AP)
First Named Inventor	John Sefton
COMPLETE IF KNOWN	
Application Number	/
Filing Date	
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

TAZAROTENE AND CORTICOSTEROID TREATMENT FOR PSORIASIS

the specification of which *(Title of the Invention)*

☐ is attached hereto
OR
☒ was filed on (MM/DD/YYYY) Feb. 20, 1998 as United States Application Number or PCT International Application Number 98/03355 and was amended on (MM/DD/YYYY) _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or 365(a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached? YES	NO
98/03355	PCT/US	02/20/1998	☐	☐	☐
			☐	☐	☒
			☐	☐	☐
			☐	☐	☐

☐ Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto:

I hereby claim the benefit under 35 U.S.C. 119(e) of any United States provisional application(s) listed below.

Application Number(s)	Filing Date (MM/DD/YYYY)
60/039,151	02/20/1997

☐ Additional provisional application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto.

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U.S. Parent Application or PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (if applicable)
PCT/US98/03355	02/20/1998	

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As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: ☐ Customer Number → [ ] Place Customer Number Bar Code Label here
OR
☒ Registered practitioner(s) name/registration number listed below

Name	Registration Number	Name	Registration Number
BARAN, Robert J.	25,806	DONOVAN, Stephen	33,433
FISHER, Carlos A.	36,510		
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☐ Additional registered practitioner(s) named on supplemental Registered Practitioner Information sheet PTO/SB/02C attached hereto.

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor: ☐ A petition has been filed for this unsigned inventor

Given Name (first and middle [if any])	Family Name or Surname
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☐ Additional Inventors are being named on the ____ supplemental Additional Inventor(s) sheet(s) PTO/SB/02A attached hereto